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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,527	08/04/2006	Masaichi Hasegawa	TC00008	8681

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EXAMINER

SZNAIDMAN, MARCOS L

ART UNIT	PAPER NUMBER
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1611

NOTIFICATION DATE	DELIVERY MODE
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09/26/2008

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/588,527	Applicant(s) HASEGAWA ET AL.	
	Examiner MARCOS SZNAIDMAN	Art Unit 1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 June 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 8-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-4 and 9 is/are allowed.
- 6) ☒ Claim(s) 8, 10 and 11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1 page / 06/06/08</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This office action is in response to applicant's reply filed on June 6, 2008.

Status of Claims

Amendment of claims 1, and 8-10; cancellation of claims 5-7, and addition of new claim 11 is acknowledged.

Claims 1-4, and 8-11 are currently pending and are the subject of this office action.

Claims 2-3 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention/species, there being no allowable generic or linking claim. Election has been treated as an election without traverse in the reply filed on December 21, 2007. Species elected by applicant: 2-(2-Amino-ethylamino)-6-quinolin-6-yl-3H-pyrimidin-4-one (example 1 on page 28 of the specification) , since the species was free of prior art, the examination was expanded to the following species: 2-[[3-(methyloxy)phenyl]amino]-6-(4-pyridinyl)-4(1H)-pyrimidinone (example 44 on page 61 of the specification) in the office action of February 6, 2008. Since applicant has cancelled the expanded species, examination was now expanded to the remaining species.

Claims 1-4 and 8-11 are currently under examination.

Priority

The present application is a 371 of PCT/US05/02972 filed on 02/03/2005, and claims priority to provisional application No. 60/542,090 filed on 02/04/2004.

Response to Arguments

This is in response to applicant's arguments, filed on June 6, 2008.

Improper restriction requirement.

Applicant argues that: "because proper restriction requirement was never issued, the entire scope of the claimed invention has already been searched and nothing in the art or record anticipates or renders obvious compounds of claim 1, applicants submits that claim 1 should not be the subject of restriction and respectfully request rejoinder of compounds of claim 3 and 4".

In the response filed on December 21, 2007, applicant elected the following species: 2-(2-Amino-ethylamino)-6-quinolin-6-yl-3H-pyrimidin-4-one (example 1 on page 28 of the specification, this species read on claims 1-2 and 5-10 of the original claims). Since the species was free of prior art, the examination was expanded to the following species: 2-[[3-(methyloxy)phenyl]amino]-6-(4-pyridinyl)-4(1H)-pyrimidinone (example 44 on page 61 of the specification, this species read on claims 5-10 of the original claims). Both species combined read on the following claims: 1-2 and 5-10, which are the claims that were examined. At no point it was mentioned that the

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examination was expanded to all the remaining species. For this reason claims 3 and 4 were withdrawn from examination in the previous office action.

Claims rejected under 35 USC 112, first paragraph (written description).

Due to applicant's amendment of claims 1, and 8-9; and cancellation of claims 5-7, the written description rejection is now moot.

Rejection under 35 USC 112, first paragraph (written description) is withdrawn.

Claims rejected under 35 USC 112, first paragraph (enablement).

Due to applicant's cancellation of claims 6 and 7, the enablement rejection for claims 6 and 7 is now moot.

Rejection under 35 USC 112, first paragraph (enablement) is withdrawn for claims 6 and 7.

Applicant's arguments regarding claim 8 have been fully considered but are not persuasive.

Despite the amendment of claim 8: removal of the terms "solvate", "derivative" and "preventing", and since applicant did not present any valid arguments, the enablement rejection against claim 8 (and newly added claim 11) is maintained.

Rejection under 35 USC 112, first paragraph (enablement) is maintained for claim 8 (and newly added claim 11).

Claims rejected under 35 USC 102 (b)

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Due to applicant's cancellation of claim 5, the 102 (b) rejection is now moot.

Rejection under 35 USC 102 (b) is withdrawn for claim 5.

Due to applicant's amendment of claim 9 (R1 can not be pyridine) the 102 (b) rejection is now moot.

Rejection under 35 USC 102 (b) is withdrawn for claim 9.

Applicant cancelled the species: 2-[[3-(methyloxy)phenyl]amino]-6-(4-pyridinyl)-4(1H)-pyrimidinone (example 44 on page 61 of the specification). However, the following species: 2-[(2-Chlorophenyl)amino]-6-(4-pyridinyl)-4(1H)-pyrimidinone (fifth compound from the bottom on claim 10, page 12, and example 41, page 59 of the specification) is taught in the prior art (Watanabe et. al. (WO2000/18758 cited by applicant, cited in prior office action, see compound 47, Table 1 on page 24) and anticipates the claim.

Rejection under 35 USC 102(b) is maintained for claim 10.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Allowable Subject Matter

Claims 1-4 and 9 allowed.

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Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8 and 11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an enablement rejection.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. *PPG v. Guardian*, 75 F.3d 1558, 1564 (Fed. Cir. 1996). As pointed out by the court in *In re Angstadt*, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) at 547 the court recited eight factors:

1- the quantity of experimentation necessary,

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- 2- the amount of direction or guidance provided,
- 3- the presence or absence of working examples,
- 4- the nature of the invention,
- 5- the state of the prior art,
- 6- the relative skill of those in the art,
- 7- the predictability of the art, and
- 8- the breadth of the claims

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the *Wands* factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention

Claims 8 and 11 describe a method of treating diseases selected from the group consisting of: anemia, aplastic anemia, myelodysplastic syndrome, etc comprising, administering to a mammal (a human in claim 11) a therapeutically effective amount of a compound of formula I (see claim 1), or a salt thereof.

2. The state and predictability of the art

It is well established that “the scope of enablement varies with the degree of unpredictability of the factors involved” and physiological activity is considered to be an unpredictable factor. See *In re Fisher*, 166 USPQ 18, at 24 (In cases involving

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unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved); *Nationwide Chemical Corporation, et. al. v. Wright, et. al.*, 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances); *Ex parte Sudilovsky* 21 USPQ2d 1702 (Applicant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable); *In re Wright* 27 USPQ2d 1510 (the physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian vaccine was uncertain).

There is currently no prior art describing any treatment of any of the diseases of the erythroid and hematopoietic systems listed in claim 8 by administering compounds of formula I (that inhibit the activity of hYAK3).

3. The relative skill of those in the art

The relative skill of those in the art is high, generally that of an M.D. or Ph.D. The artisan using Applicant's invention would generally be a physician with a M.D. degree and several years of experience.

4. The breadth of the claims

Claims 8 and 11 recite a very broad genus of diseases to be treated with a very broad genus of compounds.

5. The amount of direction or guidance provided and the presence or absence of working examples

The specification fails to disclose any data to support the fact that any of the compounds of Formula I could treat any disease listed in claim 8. The specification only provides an *in vitro* hYAK3 kinase assay. There is no cellular or *in vivo* data to corroborate that these compounds could treat any disease of the erythroid and hematopoietic systems listed in claim 8. The rationale that applicant uses to reach these conclusions is that the presence of YAK3 proteins in hematopoietic tissues, and that the RNA is expressed at significant levels in erythroid or erythropoietin responsive cells. All these arguments suggest that YAK3 might play a role in the diseases of the erythroid and hematopoietic systems, and definitively is an invitation for further research in the area. However, the arguments and the data provided in the specification do not demonstrate at all that the compounds of formula I (inhibitors of YAK3) could treat any of the diseases listed in claim 8.

6. The quantity of experimentation necessary

In the absence of previous examples in the prior art, and in the absence of experimental evidence commensurate with the scope of the claims, how is the skilled physician supposed to know how to treat, for example, a subject with anemia? Which of the many compounds encompassed by formula I is he supposed to choose among? Which of these compounds will show any real efficacy in a human? Which doses,

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formulation and or /routes of administration is he supposed to use? This would require to run in vivo animal data for several compounds, optimize the best compounds, run pre-clinical and clinical trials or testing in an assay known to correlate to clinical efficacy of such treatment. This is undue experimentation given the limited guidance and direction provided by Applicants.

Accordingly, the inventions of claims 8 and 11 do not comply with the enablement requirement of 35 U.S.C 112, first paragraph, since to practice the claimed invention a person of ordinary skill in the art would have to engage in undue experimentation with no assurance of success.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Watanabe et. al. (WO2000/18758 cited by applicant, cited in prior art).

Claim 10 recites the following compound: 2-[(2-Chlorophenyl)amino]-6-(4-pyridinyl)-4(1H)-pyrimidinone (fifth compound from the bottom on claim 10, page 12).

For claim 10, Watanabe teaches the same compound: 2-[(2-Chlorophenyl)amino]-6-(4-pyridinyl)-4(1H)-pyrimidinone (see compound 47, Table 1 on page 24).

Conclusion

Claims 8 and 10-11 are rejected, and claims 1-4 and 9 are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is

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(571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau can be reached on 571 272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/
Examiner, Art Unit 1611
September 15, 2008
/Sharmila Gollamudi Landau/

Supervisory Patent Examiner, Art Unit 1611